

## ABSTRACT

Glutathione is a low molecular weight thiol-tripeptide. Glutathione in the reduced form (GSH) is the predominant intracellular form, which acts as a strong antioxidant. However, it has low skin permeability due to the high hydrophilicity. Hence, the objective of this study was to prepare GSH by using microspheres delivery system and adding surfactant to overcome the barrier function of the skin. This research was also investigate effect of polymer and surfactant on the characteristics and release profile of GSH–alginate microspheres. GSH-Alginate Microspheres were prepared using ionotropic gelation method by aerosolisation. A randomized full factorial design was applied to prepare four different formulations of glutathione loaded alginate microspheres. The microspheres were evaluated to entrapment efficiency (EE), drug loading (DL), particle size, yield, and in vitro drug release profile to obtain an optimized formulation. A randomized full factorial design was applied for all formulations to study about effect of independent variables of polymer and crosslinker on the EE, DL, size and release. For release study, microspheres formulas were also compared to microspheres which applied into gel base. The GSH-Alginate Microspheres had a high EE ranging from  $34.74 \pm 0.07\%$  to  $56.63 \pm 0.36\%$ , with small particle sizes ranging from  $1.89 \pm 0.03 \mu\text{m}$  to  $2.42 \pm 0.08 \mu\text{m}$ , and drug loading ranging from  $5.72 \pm 0.05\%$  to  $6.23 \pm 0.02\%$ . The kinetic analysis of all release profiles was found to follow Higuchi's diffusion model. While the model of release kinetics suitable for glutathione was first order that showed release of the active ingredient depends on remaining concentration. The penetration test showed that all systems were able to penetrate the dermis layer at the 5<sup>th</sup> hour. F6-gel based had rapid onset and can penetrate farther than other. This result suggested that polymer concentration and surfactant were important for sustained release characteristics and in vitro release profile of GSH-loaded alginate microspheres. The result of glutathione effectiveness test showed F6-gel based has lowest total of macrophage ( $0.83 \pm 0.23$ ), total of fibroblast ( $37.17 \pm 1.18$ ) and very dense collagen observation (score :  $3.33 \pm 0.47$ ). From this research, it can be concluded that F6-gel based had the most optimal composition to increase the penetration and effectiveness of glutathione as antiaging.

*Keyword : glutathione-alginate microspheres, surfactant, release profile, characteristics, penetration, effectivity*